



PAX6 gene

paired box 6

Normal Function

The *PAX6* gene belongs to a family of genes that play a critical role in the formation of tissues and organs during embryonic development. The members of the PAX gene family are also important for maintaining the normal function of certain cells after birth. To carry out these roles, the PAX genes provide instructions for making proteins that attach to specific areas of DNA and help control the activity (expression) of particular genes. On the basis of this action, PAX proteins are called transcription factors.

During embryonic development, the PAX6 protein is thought to turn on (activate) genes involved in the formation of the eyes, the brain and spinal cord (central nervous system), and the pancreas. Within the brain, the PAX6 protein is involved in the development of a specialized group of brain cells that process smell (the olfactory bulb). Additionally, researchers believe that the PAX6 protein controls many aspects of eye development before birth. After birth, the PAX6 protein likely regulates the expression of various genes in many structures of the eyes.

Health Conditions Related to Genetic Changes

aniridia

More than 280 mutations in the *PAX6* gene have been found to cause aniridia, which is an absence of the colored part of the eye (the iris). Most of these mutations create a premature stop signal in the instructions for making the PAX6 protein and lead to the production of an abnormally short, nonfunctional protein. As a result, there is less PAX6 protein to regulate the activity of other genes.

The majority of mutations that cause aniridia occur within the *PAX6* gene; however, some disease-causing mutations occur in neighboring regions of DNA that normally regulate the expression of the *PAX6* gene, known as regulatory regions. Mutations in *PAX6* gene regulatory regions reduce the expression of the *PAX6* gene. These mutations lead to a shortage of functional PAX6 protein, which disrupts the formation of the eyes during development.

coloboma

Gillespie syndrome

At least two mutations in the *PAX6* gene have been identified in people with Gillespie syndrome, a disorder characterized by eye abnormalities including absence of part

of the iris (partial aniridia), difficulty coordinating movements (ataxia), and mild to moderate intellectual disability. The mutations that cause Gillespie syndrome result in the absence of the PAX6 protein or production of a nonfunctional PAX6 protein that is unable to bind to DNA and regulate the activity of other genes. This lack of functional protein disrupts embryonic development, especially the development of the eyes and brain, leading to the signs and symptoms of Gillespie syndrome.

microphthalmia

Peters anomaly

At least two mutations in the *PAX6* gene have been found to cause Peters anomaly. This condition is characterized by the abnormal development of certain structures at the front of the eye and clouding of the clear front surface of the eye (cornea). The mutations that cause Peters anomaly change single protein building blocks (amino acids) in the PAX6 protein. These mutations reduce but do not eliminate the protein's function and are less severe than mutations that cause aniridia (described above). The mutations that cause Peters anomaly reduce the PAX6 protein's ability to bind to DNA, disrupting its role as a transcription factor. As a result, normal development of the eye is impaired, leading to the features of Peters anomaly. The *PAX6* gene mutations that cause Peters anomaly can cause other related eye disorders in members of the same family.

WAGR syndrome

The *PAX6* gene is located in a region of chromosome 11 that is deleted in people with WAGR syndrome, which is a disorder that affects many body systems and is named for its main features: a childhood kidney cancer known as Wilms tumor, an eye problem called aniridia, genitourinary anomalies, and intellectual disability (formerly referred to as mental retardation). As a result of this deletion, affected individuals are missing one copy of the *PAX6* gene in each cell. A loss of the *PAX6* gene is associated with the characteristic eye features of WAGR syndrome, including aniridia, and may affect brain development.

other disorders

Mutations in the *PAX6* gene can cause eye problems other than aniridia and Peters anomaly. The mutations that cause these eye problems occur in one copy of the *PAX6* gene in each cell. Most of these mutations change single amino acids in the PAX6 protein. These mutations reduce but do not eliminate the protein's normal function, impairing its role as a transcription factor.

Individuals with these relatively mild *PAX6* gene mutations may be born with pupils that are not centrally positioned in the eye (ectopia pupillae), small eyes (microphthalmia), and underdeveloped optic nerves, structures that carry information from the eyes to the brain. Mild *PAX6* mutations can also result in a gap or split

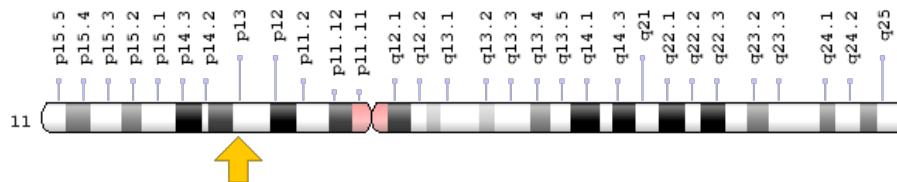
in structures that make up the eye (coloboma) or an underdeveloped region at the back of the eye responsible for sharp central vision (the fovea). Additional conditions caused by these *PAX6* gene mutations may be present at birth or develop later. These conditions may include a clouding of the lens of the eye (cataracts), involuntary eye movements (nystagmus), and inflammation of the front surface of the eye called the cornea (keratitis).

It is unclear why the effects of some mutations in the *PAX6* gene are limited to the eye, while other mutations affect the development of many parts of the body.

Chromosomal Location

Cytogenetic Location: 11p13, which is the short (p) arm of chromosome 11 at position 13

Molecular Location: base pairs 31,784,792 to 31,817,961 on chromosome 11 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- AN
- AN2
- D11S812E
- MGC17209
- MGDA
- paired box gene 6
- paired box gene 6 isoform a
- paired box gene 6 isoform b
- PAX6_HUMAN

Additional Information & Resources

Educational Resources

- Leiden University Medical Center: PAX6 Variation Database
http://lsdb.hgu.mrc.ac.uk/home.php?select_db=PAX6

GeneReviews

- Aniridia
<https://www.ncbi.nlm.nih.gov/books/NBK1360>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28PAX6%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D>

OMIM

- CATARACT 9, MULTIPLE TYPES
<http://omim.org/entry/604219>
- COLOBOMA OF OPTIC NERVE
<http://omim.org/entry/120430>
- COLOBOMA, OCULAR, AUTOSOMAL DOMINANT
<http://omim.org/entry/120200>
- ECTOPIA PUPILLAE
<http://omim.org/entry/129750>
- FOVEAL HYPOPLASIA 1
<http://omim.org/entry/136520>
- KERATITIS, HEREDITARY
<http://omim.org/entry/148190>
- OPTIC NERVE HYPOPLASIA, BILATERAL
<http://omim.org/entry/165550>
- PAIRED BOX GENE 6
<http://omim.org/entry/607108>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/PAX6ID211ch11p13.html>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=PAX6%5Bgene%5D>
- HGNC Gene Family: Paired boxes
<http://www.genenames.org/cgi-bin/genefamilies/set/675>
- HGNC Gene Family: PRD class homeoboxes and pseudogenes
<http://www.genenames.org/cgi-bin/genefamilies/set/521>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=8620
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/5080>
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<http://www.uniprot.org/uniprot/P26367>

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